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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,564	02/18/2004	James P. Quigley	1361.036US1	9290

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EXAMINER	
SANG, HONG	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/781,564	QUIGLEY ET AL.	
	Examiner	Art Unit	
	Hong Sang	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-33* is/are pending in the application.

4a) Of the above claim(s) *3-30 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/4/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

RE: Quigley et al.

1. Applicant's election of Group I (claims 1, 2, 31 and 32) in the reply filed on 4/24/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 1-33 are pending. Claims 3-30 and 33 are cancelled.

3. The information disclosure statement (IDS) filed on 8/4/05 has been considered. A signed copy is attached hereto. For the WO 02/04505 A1 document, only the abstract was considered.

4. Claims 1, 2, 31 and 32 are under examination.

Specification

5. The disclosure is objected to because of the following informality. The Brief Description of the Drawings does not reference each of the Figures. The Brief Description should be amended to reference Figures 8A and 8B. Correction is required.

Claim Rejections - 35 USC § 101

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

7. Claims 1, 2, 31 and 32 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1, 2, 31 and 32, as written,

do not sufficiently distinguish over proteins and peptides (fragments of a protein) as they exists naturally because claims do not particularly point out any non-naturally occurring differences between the claimed proteins and peptides and the naturally occurring proteins and peptides.

In the absence of the hand of man, the naturally occurring proteins and peptides are considered non-statutory subject matter (Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980)). It should be noted that the mere purity of a naturally occurring product does not necessarily impart patentability (Ex parte Siddiqui, 156 U.S.P.Q. 426 (1966)). However, when purification results in a new utility, patentability is considered (Merck Co. v. Chase Chemical Co., 273 F.Supp 68 (1967), 155 USPQ 139, (District Court, New Jersey, 1967)). Amendment of the claims to recite "an isolated" or "purified" protein or fragment or similar language would obviate this rejection.

Claim Rejections - 35 USC § 112, 1st paragraph

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 2 and 31 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

Applicants broadly claim a fragment of a protein comprising SEQ ID NO.1 that is glycosylated or non-glycosylated, and a fragment of a protein comprising SEQ ID NO.1 that is glycosylated or non-glycosylated wherein the fragment contains amino acid 525, and/or amino acid 709, and/or amino acids 827.

The invention is in a class of invention, which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

The breadth of the claims

Applicants broadly claim any fragments with or without the biological function of SEQ ID NO.1. The claims encompass undefined and uncharacterized protein fragments, which can be as small as two amino acid residues.

Quantity of experimentation

The quantity of experimentation in this area is extremely large since there is significant variability in the structure and function of protein fragments.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to any fragment with or without the biological properties of SEQ ID NO.1, and applicant has not enabled any fragments of SEQ ID NO.1 because it has not been shown that these fragments are capable of functioning as SEQ ID NO.1. The specification does not teach how to use the full scope of the fragments.

The state of the prior art and the predictability or lack thereof in the art:

Protein chemistry is probably one of the most unpredictable areas of biotechnology. It is known in the art that the relationship between the amino acid sequence of a protein (polypeptide) and its tertiary structure (i.e. its binding activity) are not well understood and are not predictable (see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz, et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495). There is no recognition in the art that sequence with identity predicts biological function. It is known in the art that even single amino acid changes or differences in a protein's amino acid sequence can have dramatic effects on the protein's function. For example, conservative replacement of a single "lysine" reside at position 118 of acidic fibroblast growth factor by "glutamic acid" led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990). In transforming growth factor alpha,

replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Furthermore, the specification fails to teach what deletions, truncations, substitutions and mutations of the disclosed sequence can be tolerated that will allow the protein to function as claimed. While it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with reasonable expectation of success are limited. Certain positions in the sequence are critical to the three-dimensional structure/function relationship, and these regions can tolerate only conservative substitutions or no substitutions. Residues that are directly involved in protein functions such as binding will certainly be among the most conserved (Bowie et al. Science, 247:1306-1310, 1990, p. 1306, col.2).

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure how to use any fragments of the protein of SEQ ID NO: 1. Therefore, in view of the lack of predictability of the prior art, the breadth of the claims and the absence of working examples, it would require undue experimentation for one skilled in the art to practice the invention as claimed.

Working examples:

The specification teaches identification of the protein of SEQ ID NO.1, and cloning of the mRNA encoding the variant of SEQ ID NO.1, wherein the amino acid 525 is glutamine, the amino acid 709 is aspartic acid, and the amino acid 827 is asparagine (see Example XII). The specification teach that the expression pattern of the protein of SEQ ID NO.1 in normal and malignant cells and tissues (see Example XIV). However, the specification does not teach any fragments of SEQ ID NO.1 and their expression in cancer cells.

Guidance in the specification

While one of ordinary skill in the art can theoretically produce all of these protein fragments with art known techniques such as site-directed mutagenesis, it would still be burdensome to one of ordinary skill in the art to produce all of these fragments and thereafter determine their activity. Moreover, the specification does not describe any fragment of SEQ ID NO.1. While the specification teaches that fragments of SEQ ID NO.1 may be used to make antibodies that bind the protein SEQ ID NO.1, the specification fails to teach which fragments would generate antibodies that specifically bind to the protein of SEQ ID No.1. Fragments as small as two amino acid residues would not generate antibodies.

Level of skill in the art

The level of the skill in the art is deemed to be high

Conclusion:

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of the art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example which teaches the protein fragments of SEQ ID NO.1 and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 2, 31 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 02/04508 A1 (Pub. Date: 1/17/2002, IDS).

Claims 2, 31 and 32 are drawn to a fragment of a protein having SEQ ID NO.1 that is glycosylated or non-glycosylated, a fragment of a protein having SEQ ID NO.1 that is glycosylated or non-glycosylated, wherein the fragment contains amino acid 525,

and/or amino acid 709, and/or amino acid 827, and a variant of a protein having SEQ ID NO.1, wherein the variant has as amino acid 525 either glutamine, has as amino acid 709 either glycine or aspartic acid, and has as amino acid either serine or asparagine.

WO 02/04508 A1 teaches a tumor associated antigen designated B345 having SEQ ID NO.4 and a fragment thereof (see claim 1, and page 85-88). Because the SEQ ID NO.4 is 99.8% identical to the instant SEQ ID NO.1, wherein the amino acid 525 is glutamine and the amino acid 827 is asparagine (see sequence alignment: Exhibit A), the teachings of WO 02/04508 A1 anticipate claims 2, 31 and 32.

12. Claims 2, 31 and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Schweifer et al. (US20020142003A1, effective filing date at least 7/6/2001).

The interpretation of claims 2, 31 and 32 are set forth above (see paragraph 12 above).

Schweifer et al. teach a tumor associated antigen designated B345 having SEQ ID NO.4 and a fragment thereof (see claim 1). Because the SEQ ID NO.4 is 99.8% identical to the instant SEQ ID NO.1, wherein the amino acid 525 is glutamine and the amino acid 827 is asparagine (see sequence alignment: Exhibit B), the teachings of Schweifer anticipate claims 2, 31 and 32.

Conclusion

13. No claims are allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hong Sang whose telephone number is (571) 272 8145. The examiner can normally be reached on 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry R. Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Hong Sang
Art Unit 1643
May 11, 2006

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER